

National Institute on Drug Abuse http://www.drugabuse.gov/

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Combination of Genes and Prenatal Exposure to Smoking Increases Teens' Risk of Disruptive Behavior

NIDA Study Shows Different Gene Variants Influence this Risk for Girls and Boys

A study funded by the National Institute on Drug Abuse, a component of the National Institutes of Health, shows that prenatal exposure to smoking *combined* with a specific genetic variant places children at greatest risk for behavioral problems. Many studies have established that there is an increased risk of aggressive behavior in children exposed to cigarette smoke before birth, a significant problem given that many women still smoke during pregnancies. According to the National Survey on Drug Use and Health, in 2006-2007 slightly more than 16 percent of pregnant women aged 15-44 (426,000) were current cigarette smokers.

A team of researchers led by the Institute for Juvenile Research, University of Illinois at Chicago, identified a long-lasting influence on behavior of the monoamine oxidase A (MAOA) gene variant following tobacco exposure before birth. MAOA is an enzyme which regulates key neurotransmitters*, or chemical messengers in the brain. Strikingly, the genetic variant that confers this increased risk differs between boys and girls.

"These findings illuminate how the interaction between genes and the environment can mold behavioral patterns very early in development," said NIDA Director Dr. Nora Volkow. "This research provides a foundation for studies of the impact of these interactions on brain development during pregnancy."

The researchers studied 176 non-Hispanic white youth, whose average age was 15, and their biologic mothers. In contrast with previous studies of prenatal smoking that have measured exposure based on the mother's recollection of past smoking, this study obtained accurate measurements of smoking behaviors during the actual pregnancy.

In boys, with the low-activity MAOA (*MAOA-L*) gene variant, exposure to prenatal smoking was associated with increased disruptive social interactions, including aggressive behaviors and serious rule-violating. "Low activity" means that the gene produces less of its product, the enzyme monoamine oxidase A. In contrast, exposure to prenatal smoking was associated with increased disruptive behavior in girls who had the high-activity MAOA (*MAOA-H*) variant. For

both boys and girls, the more their mothers had smoked during pregnancy, the higher the risk of disruptive behavior.

Additionally, on computerized tasks, girls with both the *MAOA-H* variant and prenatal exposure to smoking had a greater tendency to perceive anger in a range of facial expressions, a tendency that researchers term "hostile attribution bias." This effect was not seen among boys.

"The tendency to over-perceive anger suggests the possibility that the combination of prenatal tobacco exposure and the MAOA risk variant affects the brain's processing of emotional cues," said the study's principal investigator, Dr. Lauren S. Wakschlag, associate professor of psychiatry at the Institute for Juvenile Research, University of Illinois at Chicago. "Individuals with a greater tendency to perceive hostility in others are more likely to respond aggressively. These findings provide us with clues to the possible mechanism by which prenatal exposure may exert its effects on brain and behavior. Clearly, close attention to sex differences in these patterns will be critical for future studies."

Dr. Wakschlag led the study in collaboration with colleagues from the Institute for Juvenile Research as well as researchers from the National Institute of Mental Health (which is also a component of the National Institutes of Health); the University of Chicago; Harvard University Medical School; and the University of York, England.

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^{*} i.e., dopamine, epinephrine, norepinephrine, serotonin